AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all prior versions:

1-20. (canceled)

21. (previously presented): A vector comprising:

(1) a nucleic acid encoding a chimeric nuclease that comprises:

(i) a zinc finger DNA binding domain;

(ii) a cleavage domain; and

(iii) a nuclear localization signal; and

(2) a nucleic acid comprising a repair substrate that comprises:

(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and

(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

22-27. (canceled)

28. (currently amended): An isolated mammalian cell comprising:

(a) a chimeric nuclease comprising a zinc finger DNA-binding domain and a cleavage domain; and

(b) a repair substrate comprising

(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in endogenous chromosomal DNA; and

(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

29-39. (canceled)

40. (currently amended): An isolated mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate, wherein the chimeric nuclease comprises:

(i) a zinc finger DNA binding domain; and

(ii) a cleavage domain,

and wherein the repair substrate comprises:

(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in endogenous chromosomal DNA; and

(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

41-42. (canceled)

43. (withdrawn): A method of changing a target sequence in endogenous chromosomal DNA of a mammalian cell, comprising:

(a) introducing a chimeric nuclease into the cell, wherein said chimeric nuclease comprises:

(i) a zinc finger DNA binding domain; and

(ii) a cleavage domain; and

(b) introducing a repair substrate into the cell, wherein said repair substrate comprises:

(i) a nucleic acid sequence that is substantially identical to a region surrounding the target sequence; and

(ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence, whereby the target sequence is changed by the repair substrate upon recombination.

44-98. (canceled)

99. (previously presented) The vector of claim 21, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter.

100. (previously presented): The vector of claim 99, wherein the promoter is an inducible promoter.

101. (previously presented): The vector of claim 99, wherein the vector is a viral vector.

102. (previously presented): The vector of claim 21, further comprising a nucleic acid encoding a second chimeric nuclease, wherein the second chimeric nuclease forms a heterodimer with said chimeric nuclease.

103. (previously presented): The cell of claim 28, wherein the chimeric nuclease is encoded by a nucleic acid that is operably linked to a promoter.

104. (previously presented): The vector of claim 103, wherein the promoter is an inducible promoter.

105-106. (canceled)

107. (previously presented): The cell of claim 28, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

108. (previously presented): The cell of claim 107, wherein the cleavage domain comprises a FokI cleavage domain.

109. (withdrawn): The method of claim 43, wherein the target sequence contains an allele that contributes to a disease that is repaired by the repair substrate.

110. (withdrawn): The method of claim 43, wherein the target sequence is situated in a gene that is attenuated or inactivated by the repair substrate.

111. (withdrawn): The method of claim 43, wherein the target sequence is replaced by a heterologous sequence in the repair substrate.

112. (withdrawn): The method of claim 111, wherein the heterologous sequence comprises the coding sequence of a transgene.

113. (withdrawn): The method of claim 111, wherein the target sequence is selected such that the coding sequence of the transgene is inserted at a transcriptionally active site.

114-119. (canceled)

120. (withdrawn): The method of claim 43, wherein the cleavage domain comprises a cleavage domain of a restriction endonuclease.

121. (withdrawn): The method of claim 120, wherein the cleavage domain comprises a FokI cleavage domain.

122. (withdrawn): The method of claim 43, wherein the chimeric nuclease forms a heterodimer of two different chimeric nuclease.

123. (withdrawn): The method of claim 43, wherein the target sequence includes an allele that participates in the causation of a disease.

124. (withdrawn): The method of claim 43, wherein the repair substrate is operably linked to a promoter.

125. (withdrawn): The method of claim 124, wherein the promoter is an inducible promoter.

126. (withdrawn, currently amended): The method of claim 43, wherein the target sequence is ~~a~~ endogenous to the cell.

127. (withdrawn): A method of changing a target sequence in endogenous chromosomal DNA of a mammalian cell, comprising:

(a) introducing a nucleic acid encoding a chimeric nuclease into the cell, wherein said chimeric nuclease comprises:

(i) a zinc finger DNA binding domain;

(ii) a cleavage domain; and

(iii) a nuclear localization signal;

whereby the chimeric nuclease is produced in the cell; and

(b) introducing a nucleic acid comprising a repair substrate into the cell, wherein said repair substrate comprises:

(i) a nucleic acid sequence that is substantially identical to a region surrounding the target sequence; and

(ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,

whereby the target sequence is changed by the repair substrate upon recombination.

128. (withdrawn): The method of claim 127, wherein the target sequence contains an allele that contributes to a disease that is repaired by the repair substrate.

129. (withdrawn): The method of claim 127, wherein the target sequence is situated in a gene that is attenuated or inactivated by the repair substrate.

130. (withdrawn): The method of claim 127, wherein the target sequence is replaced by a heterologous sequence in the repair substrate.

131. (withdrawn): The method of claim 130, wherein the heterologous sequence comprises the coding sequence of a transgene.

132. (withdrawn): The method of claim 130, wherein the target sequence is selected such that the coding sequence of the transgene is inserted at a transcriptionally active site.

133. (withdrawn): The method of claim 127, wherein the nucleic acid encoding the chimeric nuclease and the repair substrate are present in a single vector introduced into the cell.

134. (withdrawn): The method of claim 127, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter in a vector.

135. (withdrawn): The method of claim 134, wherein the promoter is an inducible promoter.

136. (canceled)

137. (withdrawn): The method of claim 127, wherein the cleavage domain comprises a cleavage domain of a restriction endonuclease.

138. (withdrawn): The method of claim 137, wherein the cleavage domain comprises a FokI cleavage domain.

139. (withdrawn): The method of claim 127, wherein the chimeric nuclease forms a heterodimer of two different chimeric nuclease.

140. (withdrawn): The method of claim 127, wherein the target sequence includes an allele that participates in the causation of a disease.

141. (withdrawn): The method of claim 127, wherein the repair substrate is operably linked to a promoter.

142. (withdrawn): The method of claim 141, wherein the promoter is an inducible promoter.

143. (withdrawn): The method of claim 43, wherein the target sequence is endogenous to the cell.